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L9 ANSWER 9 OF 76 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1997:263843 BIOSIS
DN PREV199799570446
TI Chelation and mobilization of cellular iron by different classes of
chelators.
AU Zanninelli, G.; Glickstein, H.; Breuer, W.; Milgram, P.; Brissot, P.;
Hider, R. C.; Konijn, A. M.; Libman, J.; Shanzer, A.; Cabantchik, Z. Ioav
(1)
CS (1) Dep. Biological Chemistry, Inst. Life Sci., Hebrew Univ. Jerusalem,
Jerusalem 91904 Israel
SO Molecular Pharmacology, (1997) Vol. 51, No. 5, pp. 842-852.
ISSN: 0026-895X.
DT Article
LA English
AB **Iron chelators** belonging to three distinct chemical
families were assessed in terms of their physicochemical properties and
the kinetics of iron chelation in solution and in two biological systems.
Several hydroxypyridinones, reversed siderophores, and desferrioxamine
derivatives were selected to cover agents with different iron-binding
stoichiometry and geometry and a wide range of lipophilicity, as
determined by the octanol-water partition coefficients. The selection
also included highly lipophilic chelators with potentially **cell**
-cleavable ester groups that can serve as precursors of hydrophilic and
membrane-impermeant **chelators**. **Iron** binding was
determined by the chelator capacity for restoring the fluorescence of
iron-quenched calcein (CA), a dynamic fluorescent metallosensor. The
iron-scavenging properties of the chelators were assessed under three
different conditions: (a) in solution, by mixing iron salts with free CA;
lb) in resealed red **cell** ghosts, by encapsulation of CA followed
by loading with iron; and (c) in human erythroleukemia K562 **cells**
, by loading with the permeant CA-acetomethoxy ester, in situ formation
of free CA, and binding of cytosolic labile iron. The time-dependent
recovery of fluorescence in the presence of a given chelator provided a continuous
measure for the capacity of the **chelator** to access the
iron/CA-containing compartment. The resulting rate constants of
fluorescence recovery indicated that chelation in solution was comparable
for the members of each family of chelators, whereas chelation in either
biological system was largely dictated by the lipophilicity of the free
chelator. For example, desferrioxamine was among the fastest and most
efficient iron scavengers in solution but was essentially ineffective in
either biological system when used at $200 \mu\text{M}$ over a 2-hr period
at 37 degree . On the other hand, the highly lipophilic and potentially
cell-cleavable hydroxypyridinones and reversed siderophores were
highly efficient in all biological systems tested. It is implied that in
K562 **cells**, hydrolysis of these chelators is relatively slower
than their ingress and binding of intracellular **iron**. The
chelator-mediated translocation of **iron** from
cells to medium was assessed in ^{55}Fe -**transferrin**
-loaded K562 **cells**. The speed of iron mobilization by members of
the three families of chelators correlated with the lipophilicity of the
free ligand or the **iron-complexed chelator**.
The acquired information is of relevance for the design of chelators with
improved biological performance.

L9 ANSWER 72 OF 76 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1984:273093 BIOSIS
DN BA78:9573
TI A LIPOPHILIC **IRON CHELATOR** CAN REPLACE
TRANSFERRIN AS A STIMULATOR OF **CELL** PROLIFERATION AND
DIFFERENTIATION.
AU LANDSCHULZ W; THESLEFF I; EKBLUM P
CS DEP. PATHOLOGY, UNIV. HELSINKI, HAARTMANINKATU 3, SF-00290 HELSINKI 29,
FINL.
SO J CELL BIOL, (1984) 98 (2), 596-601.
CODEN: JCLBA3. ISSN: 0021-9525.
FS BA; OLD
LA English
AB Of the different growth supplements used in chemically defined
media, only **transferrin** is required for differentiation
of tubules in the embryonic mouse metanephros. Since **transferrin**
is an Fe-carrying protein, the crucial role of Fe for tubulogenesis was
determined. Differentiation of metanephric tubules in whole embryonic
kidneys and in a transfilter system was studied. The tissues were grown
in chemically defined **media** containing **transferrin**,
apotransferrin, the metal-chelator complex ferric pyridoxal isonicotinoyl
hydrazone (FePIH) and excesses of Fe³⁺. Although apotransferrin was not
as effective as Fe-loaded **transferrin** in promoting proliferation in
the differentiating kidneys, excess Fe³⁺ at up to 100 .mu.M, 5 times the
normal serum concentration, could not promote differentiation or
proliferation. Fe coupled to the nonphysiological, lipophilic **iron**
chelator, pyridoxal isonicotinoyl hydrazone, to form FePIH, could
sustain levels of **cell** proliferation and tubulogenesis similar
to those attained by **transferrin**. The role of
transferrin in **cell** proliferation during tubulogenesis
is solely to provide Fe. Since FePIH apparently bypasses the
receptor-mediated route of Fe intake, the use of FePIH as a tool for
investigating **cell** proliferation and its regulation is
suggested.

Stone @ Brock

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AN 1987:359060 BIOSIS

DN BA84:56463

TI REPLACEMENT OF **TRANSFERRIN** IN SERUM-FREE CULTURES OF MITOGEN
STIMULATED MOUSE LYMPHOCYTES BY A LIPOPHILIC **IRON**
CHELATOR.

AU BROCK J H; STEVENSON J

CS UNIV. DEP. BACTERIOLOGY AND IMMUNOLOGY, WESTERN INFIRMARY, GLASGOW G11
6NT, U.K.

SO IMMUNOL LETT, (1987) 15 (1), 23-26.
CODEN: IMLED6. ISSN: 0165-2478.

FS BA; OLD

LA English

AB Proliferation of mouse lymph node lymphocytes in response to concanavalin
A in serum-free **medium** is normally dependent upon the presence
of **transferrin**. In the absence of **transferrin**, little
proliferation occurred, but the response was restored by addition of the
iron complex of pyridoxal isonicotinoyl hydrazone
(FePIH), a lipophilic **iron chelator**. Since cellular
acquisition of PIH-bound iron is known not to involve the
transferrin receptor, these results indicate that
transferrin promotes lymphocyte proliferation solely because of
its iron-donating properties, and does not provide any additional
signaling event for proliferation.